

## Structure of the Norditerpene Ponalactone A and its Glucoside, Plant Growth Inhibitors

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**Summary** Structures (I) and (V) have been established, respectively, for ponalactone A and its glucoside; both exhibit plant growth inhibitory activities.

THE leaves of *Podocarpus nakaii* HAY. provided one of the first sources of phytoecdysones,<sup>1</sup> of which about forty are known.<sup>2</sup> The root yielded a new norditerpene,<sup>3</sup> in addition to ponasterone A<sup>1</sup> and C<sup>4</sup>. The present communication deals with the structure determination of this norditerpene, designated ponalactone A, to which we assign structure (I), *i.e.*, (Ia).

Ponalactone A, (I), C<sub>19</sub>H<sub>22</sub>O<sub>6</sub>, M<sup>+</sup> at *m/e* 346, m.p. 266—269° (decomp.) has the following spectral properties: i.r. (KBr) 3550 (OH), 1768 ( $\gamma$ -lactone), 1703 and 1643 cm<sup>-1</sup> (dienolide);<sup>5</sup> u.v. (MeOH) 262 ( $\epsilon$  12,500) and 227sh nm (*ca.* 7000)<sup>5</sup>; c.d. (MeOH)  $\Delta\epsilon_{262} = 9.6$ . Ponalactone A gave a monoacetate, m.p. >300°, which showed no OH absorption in the i.r. Ponalactone also gave a monoketone by Jones'

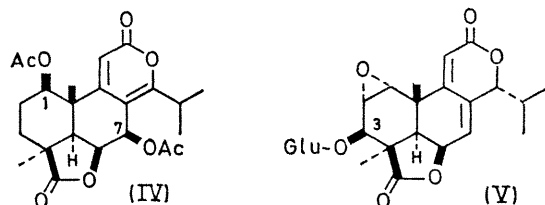
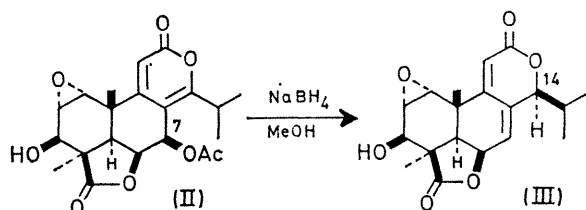
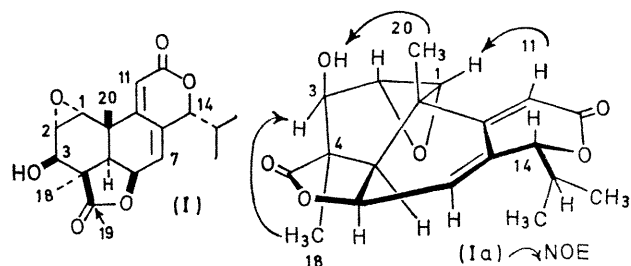
oxidation: monoketone, m.p. 289—290°, i.r. (KBr) 1780 ( $\gamma$ -lactone), 1722 (ketone), and 1708 and 1610 cm<sup>-1</sup> (dienolide). Detailed n.m.r. measurements of ponalactone A (I) coupled with double resonance techniques and comparisons

### NOE measurements of ponalactone A (I) in (CD<sub>3</sub>)<sub>2</sub>SO

Proton irradiated	Chemical shift	Proton observed	Chemical shift	% Increase of the integrated area
11-H	6.19	1-H	3.59	+23
18-H	1.37	3-H	4.27	+10
20-H	1.05	3-OH	5.30	+8

with n.m.r. data of other known norditerpenes<sup>3,6,7</sup> revealed the nature of all protons, which can be represented by the two structural moieties A and B and two tertiary methyl groups. In addition to these two partial structures, the

three NOE's observed (see Table) show that A and B can only be connected as represented by (Ia) = (I). Furthermore, the two NOE's between 18-H/3-H and 20-H/3-OH uniquely define the configurations at chiral centres 1, 2, 3, 4, and 10, and also indicate that ring A adopts a boat conformation [see (Ia)].



The structure derived for ponalactone A was expected to be identical with or closely related to that of (III), which was prepared from nagilactone C 7-acetate (II) by reduction with sodium borohydride. [This reduction was reported by Hayashi *et al.*<sup>7</sup> on nagilactone A acetate (IV), but the stereochemistry of the product was left undefined.] The resultant dienolide (III), m.p. 236–238°, i.r. (KBr) 1778 ( $\gamma$ -lactone), 1711 and 1610  $\text{cm}^{-1}$  (dienolide); u.v. (MeOH) 263 nm ( $\epsilon$  13,100) and 230sh nm (*ca.* 8300); c.d. (MeOH)  $\Delta\epsilon_{258} - 9.9$ , had an n.m.r. spectrum which was similar to that of ponalactone A (I). The only difference was the slight downfield shifts of the protons at positions 14, 16, and 17 in (III) as compared to the peaks in ponalactone A [in  $(\text{CD}_3)_2\text{SO}$ ]. In addition, in ponalactone A there were observed allylic and homoallylic couplings (between 7- and

14-H and 6- and 14-H, respectively); however, this was not the case in the n.m.r. spectrum of (III). This suggests that (I) and (III) are 14-epimers, and that (I) has an axial hydrogen at C-14. The relative structures of both epimers are thus established.

The gross absolute configurations of the two compounds

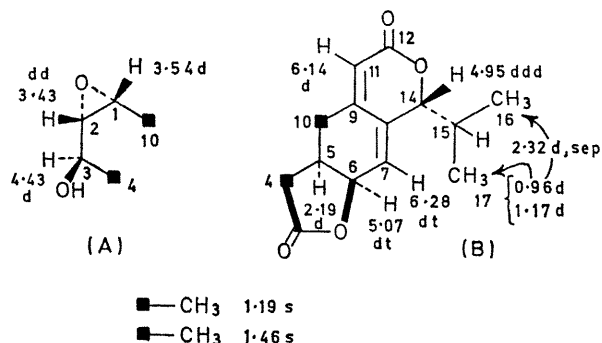


FIGURE. Part structures of ponalactone A (I).

Coupling constants (in Hz)  $J_{1,2}$  4.0,  $J_{2,3}$  6.0,  $J_{5,6}$  5.0,  $J_{6,7}$  5.0,  $J_{6,14}$  1.7,  $J_{7,11}$  2.0,  $J_{7,14}$  2.0,  $J_{14,15}$  2.5,  $J_{15,16}$  6.5,  $J_{15,17}$  6.5. Chemical shifts were obtained in  $\text{CDCl}_3$ - $(\text{CD}_3)_2\text{SO}$  solution (80:20) and are represented in p.p.m. from  $\text{Me}_4\text{Si}$ . Blocks (■) denote the carbons which carry no hydrogens.]

(I) and (III) are identical, because of the similarity in the c.d. data described here. As the absolute configuration of nagilactone C (II; 7-OH instead of 7-OAc) is known,<sup>8</sup> ponalactone A can be fully represented by (I).

A more polar component, ponalactone A glucoside, (V),  $\text{C}_{25}\text{H}_{32}\text{O}_{12}$ , m.p. 300°, i.r. (KBr) 3450 (OH), 1770 ( $\gamma$ -lactone), 1705 and 1610  $\text{cm}^{-1}$  (dienolide), u.v. (MeOH) 262 nm ( $\epsilon$  15,000), was also isolated from the roots. The n.m.r. spectrum of its tetra-acetate, m.p. 242° (decomp.), exhibited four acetate peaks, which could be assigned to a glucosidic moiety. Accordingly, the free "glucoside" was subjected to acid hydrolysis which resulted in the production of glucose and ponalactone A (identified by paper chromatography and t.l.c., respectively). The large coupling constant ( $J$  7.5 Hz at 5.19 p.p.m. in  $\text{C}_6\text{D}_6\text{N}$ ) of the signal in the n.m.r. spectrum of (IV) disclosed the axial nature of the anomeric hydrogen. The more polar component is therefore, ponalactone A 3 $\beta$ -glucoside.

Both compounds are potent inhibitors against expansion and mitosis of plant cells.<sup>9</sup>

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